COVID-19 among patients with Behçet syndrome in the USA

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Key Points

- Patients with Behçet syndrome were not at an increased risk of worse COVID-19 outcomes compared to the general population in the USA.

Dear Editor,

Behçet syndrome is a chronic multisystem condition that is characterized by relapsing–remitting periods of a diverse spectrum of manifestations [1]. Although it is more common along the ancient Silk Road [1], it is a rare syndrome with a prevalence of 5.2 per 100,000 in the USA [2]. During the COVID-19 pandemic, concerns have been raised about whether patients with Behçet syndrome are at an increased risk of worse COVID-19 outcomes. To address these concerns, small case series of 4 and 10 Behçet syndrome patients with COVID-19 have been reported from Spain [3] and Turkey [4], respectively. Moreover, 14 Behçet syndrome patients with COVID-19 have been reported from Italy [5]. In addition, in a digital conference, experts from ten countries reported the hospitalization, ICU admission, and case fatality rate of Behçet syndrome patients with COVID-19 in their hospitals or countries [6]. There is a need for a systematic study, which includes large-scale nationwide data, to increase our understanding regarding the risk of worse COVID-19 outcomes in Behçet syndrome.

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In this retrospective comparative cohort study, we used the TriNetX database, which contains de-identified electronic health records of more than 73 million persons from 53 US healthcare organizations. We included all adults (aged ≥ 18 years) with a pre-existing diagnosis of Behçet syndrome (M35.2) who were diagnosed with COVID-19 between January 20, 2020 (first confirmed COVID-19 case in the USA) and June 18, 2021. The comparative cohort included adult COVID-19 patients without Behçet syndrome. The primary outcomes of interest were hospitalization and severe COVID-19, which was defined as a composite outcome of mortality, intensive care unit admission, mechanical ventilation, acute kidney injury, acute respiratory distress syndrome, ischemic stroke, venous thromboembolism, and/or sepsis, within 45 days of COVID-19 diagnosis. We used 1:1 propensity score matching and calculated risk ratios and 95% confidence interval (CI). The database and statistical analyses that we used have been detailed previously [7, 8].

The cohort consisted of 141 Behçet syndrome with COVID-19 and 864,533 COVID-19 patients without Behçet syndrome. Patients with Behçet syndrome were of a similar age and more likely to be female (consistent with the general epidemiology of Behçet syndrome in the USA [2, 9]) compared to the comparative cohort. A majority of Behçet syndrome patients (58%) were prescribed glucocorticoids, with 18% colchicine, and 12% azathioprine in the preceding year of COVID-19 diagnosis. The hospitalization rate was 18% in the Behçet syndrome cohort. The risk of hospitalization and severe COVID-19 did not significantly differ between Behçet syndrome with COVID-19 and the comparative cohort both in unadjusted and propensity score matching analyses (Table 1).

In conclusion, we found that patients with Behçet syndrome were not at an increased risk of worse COVID-19 outcomes compared to the general population in the USA.

Although this was a large national study, it has limitations including possible errors in coding/data entry, which are inherent limitations of studies using electronic health records. In addition, most of the patients with Behçet

Table 1 Baseline characteristics, comorbidities, and COVID-19 outcomes in cohorts before and after propensity matching*

Baseline characteristic	Before propensity matching			After propensity matching		
	Behçet with COVID-19 (n = 141)	Non-Behçet with COVID-19 (n = 864,854)	Standardized difference	Behçet with COVID-19 (n = 141)	Non-Behçet with COVID-19 (n = 141)	Standardized difference
Age, years	46.8 ± 15.3	47.6 ± 18.5	0.0459	46.8 ± 15.3	48.5 ± 16.3	0.1044
Female sex‡	104 (73.759%)	474,189 (54.829%)	0.403	104 (73.759%)	104 (73.759%)	< 0.0001
Race‡						
White	93 (65.957%)	500,387 (57.858%)	0.1674	93 (65.957%)	97 (68.794%)	0.0605
Black	16 (11.348%)	142,730 (16.503%)	0.1493	16 (11.348%)	12 (8.511%)	0.095
Asian	< 11† (NA%)	18,721 (2.165%)	0.2362	< 11† (NA%)	< 11† (NA%)	< 0.0001
BMI, kg/m ²	28.7 ± 6.43	30.6 ± 7.51	0.2673	28.7 ± 6.43	32.2 ± 7.99	0.473
Hypertension	57 (40.426%)	214,607 (24.814%)	0.3377	57 (40.426%)	59 (41.844%)	0.0288
Chronic lower lung disease	39 (27.66%)	122,287 (14.14%)	0.3372	39 (27.66%)	42 (29.787%)	0.047
Diabetes mellitus	25 (17.73%)	103,657 (11.985%)	0.1621	25 (17.73%)	25 (17.73%)	< 0.0001
Ischemic heart disease	11 (7.801%)	63,510 (7.343%)	0.0173	11 (7.801%)	< 11†	NA
Chronic kidney disease	15 (10.638%)	44,681 (5.166%)	0.2039	15 (10.638%)	< 11†	NA
Heart failure	< 11†	36,016 (4.164%)	NA	< 11†	< 11†	NA
Cerebrovascular disease	13 (9.22%)	38,242 (4.422%)	0.1912	13 (9.22%)	< 11†	NA
Nicotine dependence	21 (14.894%)	60,335 (6.976%)	0.2558	21 (14.894%)	24 (17.021%)	0.0581
Alcohol-related disorders	< 11†	19,827 (2.293%)	NA	< 11†	< 11†	NA
Neoplasms	48 (34.043%)	151,908 (17.565%)	0.3835	48 (34.043%)	38 (26.95%)	0.1545
Interstitial lung disease	< 11†	3,213 (0.372%)	NA	< 11†	< 11†	NA
COVID-19 outcomes						
Outcome	Before propensity matching			After propensity matching		
	Behçet with COVID-19 (n = 141)	Non-Behçet with COVID-19 (n = 864,854)	Risk ratio (95% CI)/p value	Behçet with COVID-19 (n = 141)	Non-Behçet with COVID-19 (n = 141)	Risk ratio (95% CI)/p value
Hospitalization	26 (18.440%)	132,129 (15.278%)	1.207 (0.853, 1.708) p: 0.2967	26 (18.440%)	19 (13.475%)	1.368 (0.795, 2.357) p: 0.2550
Severe COVID-19§	13 (9.220%)	75,483 (8.728%)	1.056 (0.629, 1.773) p: 0.8360	13 (9.220%)	12 (8.511%)	1.083 (0.512, 2.291) p: 0.8341

*Data are mean ± standard deviation or number (percentage). Age, sex, race, body mass index (BMI), and comorbidities (hypertension, chronic lower lung disease, diabetes mellitus, ischemic heart disease, chronic kidney disease, heart failure, cerebrovascular disease, nicotine dependence, alcohol-related disorders, neoplasms, and interstitial lung disease, which were defined through International Classification of Diseases codes) were included as covariates in propensity score matching

†TriNetX obfuscates the number if the event count is less than 11 for privacy reasons

‡Sex data were unknown for 4 (2.8%) Behçet patients. Race data were unknown for 29 (20.6%) Behçet patients and the other races (e.g., Native Hawaiian/Pacific Islander) were obfuscated due to less than 11. Percentage data are among all patients in each cohort (not on available data)

§Composite outcome of mortality, intensive care unit admission, mechanical ventilation, acute kidney injury, acute respiratory distress syndrome, ischemic stroke, venous thromboembolism, and/or sepsis

syndrome were women, and their clinical characteristics could not be evaluated as the database did not provide this information. Furthermore, because Behçet syndrome is less severe in the USA than in endemic areas [1, 9], US results

may not be generalizable to regions where Behçet syndrome is endemic and more severe.

Author contribution HP, RR, and SK designed the study. HP and RR carried out statistical analyses. All authors contributed to interpretation of data. SK drafted the manuscript. HP, RR, and SK critically revised the article.

Declarations

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